EPIGENESIS
PHARMACEUTICALS

7 Clarke Drive
Cranbury, New Jersey 08520
*Telephone:* (609) 409-6080
*Direct Facsimile:* (413) 254-9245
*Main Facsimile:* (609) 409-6126

# FAX COVER SHEET

To: Dr. Janet Epps Company: US PTO –GAU 1635 Fax No: 703-305-7939

FROM: Viviana Amzel DATE: 5/24/01 TIME: _____

Direct Dial: (409) 609-3035 E-Mail: vamzel@epigene.com

TOTAL NO. OF PAGES: 5 Ref. No.: USSN 09/093,972 (EPI-00672)
(including cover page)

## CONFIDENTIALITY NOTICE



## COMMENTS

Further to our telephone conference of earlier today, I am nclosing a Supplemental Amendment to correct typographical\clerical errors in the specification as well as a substitute page 38. Thanks.

#36/G
BP
5-28-01
(NF)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

| | | | |
|---|---|---|---|
| Applicant: | Jonathan W. Nyce | : Art Unit: | 1635 |
| Serial No.: | 09/093,972 | : Examiner: | Dr. Epps |
| Filed: | June 9, 1998 | :Appl. Ref. No.: | EPI-00672 |

For: **COMPOSITION, FORMULATIONS & METHOD FOR PREVENTION & TREATMENT OF DISEASES AND CONDITIONS ASSOCIATED WITH BRONCHOCONSTRICTION, ALLERGY(IES) & INFLAMMATION**

## SUPPLEMENTAL AMENDMENT

I hereby certify that this correspondence is being faxed at 703-305-7939, to the Assistant Commissioner for Patents, Washington DC 20231 on May 22, 2001, by Viviana Amaya

SIGNATURE

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir/Madam:

Supplemental to the Response to the Office Action of November 7, 2000, filed March 28, 2001, Supplemental Amendments of March 28 and May 24, 2001, a 3-month extension of time and a Notice of Appeal having been filed and the respective fees paid, please amend the the specification of the above identified patent application as follows.

Do Not Enter
JLE

## IN THE SPECIFICATION

Please amend the specification as follows.

Paragraph bridging pages 37 and 38, change as follows:

In the anti-sense oligonucleotides of the present invention, exemplified by the preceding sequences, a number of adenosine bases may be replaced with an appropriate "spacer" or universal base, [(] e.g., 1-[β-D-2'-deoxyribofuranosyl]-5-nitroindole], or with an adenosine agonist or antagonist that does not stimulate adenosine $A_1$, $A_{2b}$ or $A_3$ receptors, but which may stimulate adenosine $A_{2a}$ receptors. In this manner, a specific adenosine receptor gene may be targeted to obtain one or more anti-sense oligonucleotide(s) (oligos) that selectively bind(s) to the corresponding mRNA, and then, if necessary, their content of adenosine may be reduced by substituting one or more universal bases or adenosine analogues incapable of activating adenosine $A_1$, $A_{2b}$ or $A_3$ receptors or which activate the adenosine $A_{2a}$ receptor. Thus, in addition to "down-regulating" specific adenosine receptor genes, the present oligos have an increased effect when administered by either selection of genes, RNA and flanking regions that are devoid, or have a low [A] T/U content, or alternatively one or more of the adenosine(s) present in the